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Linked comment for Lancet Psychiatry

CBT as a valid alternative to antipsychotic medication for psychosis? Possibly so, possibly not...

**Sameer Jauhar
MRCPsych
Senior Research Fellow,
Institute of Psychiatry, Psychology and Neuroscience,
King's College,
London**

Email: Sameer.jauhar@kcl.ac.uk

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For the last 60 years the mainstay of treatment for people with psychotic illness has been antipsychotic drugs¹. Antipsychotics, however, are not usually fully effective, and are associated with side-effects, ranging from weight gain/metabolic syndrome to the irreversible movement disorder of tardive dyskinesia. The last twenty years have therefore seen exploration of possible benefits of modern psychological interventions, the most studied being cognitive behavioural therapy (CBT), examined in at least 50 trials², and currently recommended by NICE.³

In the COMPARE trial, Professor Morrison and colleagues conducted a feasibility randomised controlled trial (RCT) of CBT versus antipsychotic monotherapy, and combination of both antipsychotics and CBT, in predominantly people with first episode psychosis (FEP). The trial follows their similar trial of CBT in people with established schizophrenia, who refused antipsychotic treatment⁴. In the earlier study the authors concluded it was, “a preliminary trial, which needs to be followed up by a larger, pragmatic multicentre study”, accepting it was not designed to test effectiveness, some of the CBT group going on to take antipsychotics.⁵

In the current study they recruited 75 people with predominantly FEP, not receiving treatment for at least 3 months. Prior antipsychotic treatment is unclear. Participants were given either up to 26 weekly CBT as monotherapy, antipsychotic monotherapy (varying doses, as per clinical practice) or a combination of both, for 6 months. Primary outcomes were feasibility and PANSS total scores at one year. Statistical modelling revealed a significantly worse outcome for CBT monotherapy compared to combined intervention, and trend towards worse outcome for antipsychotic monotherapy. The authors report no appreciable increase in serious adverse events, and less side effects in the CBT group (though acknowledge this was due to improvement in the scale for the CBT group, as opposed to worsening in those treated with antipsychotics).

Methodologically, it is unclear how people were diagnosed with psychosis (it seems significant numbers were included by virtue of attending FEP services), and no substance misuse history was reported. This raises issues of heterogeneity- treatment response and symptom fluctuations vary, especially in FEP, and with substance misuse. Some people may not require long-term antipsychotics (or much input at all), e.g. those with transient psychotic symptoms. This is reflected in the as-treated analysis, 5/13 people receiving no intervention having symptomatic response. With no psychosocial placebo, it is difficult to tease out effects in the CBT monotherapy group.

What is puzzling is how badly all groups fared. Meta-analysis of over 50 studies⁶ suggests 58% of people with FEP achieve functional and symptomatic remission (symptomatic remission being eight PANSS items rated “mild or better.”) Here, response criteria was >50% improvement in PANSS total⁷, which, if anything gives higher response rates than symptomatic remission⁷. The as-treated analysis (Table 5) shows 0/21 antipsychotic monotherapy, 6/20 (CBT monotherapy) and 4/21 (combined) people fulfilled response criteria at one year- around 16%.

A possible clue is that it is unclear how many people prescribed antipsychotics were actually concordant- self-report (used in this trial) is not accurate, a good example being significant numbers of people attending services for treatment resistant psychoses having

undetectable blood antipsychotic levels⁷. In addition, antipsychotic doses appear not to have increased, despite non-response, and clozapine was not considered in anyone, despite clinical guidelines on this.^{1,8}

It appears we may therefore be lacking a valid active control group, and no psychosocial placebo group to measure possible non-specific effects of therapy, and symptom fluctuations.

The authors should be congratulated on recruiting to target, demonstrating a trial like this is possible within the NHS.

Where do we go from here?

It would constitute what some may consider a Kuhnian paradigm shift for people with first onset psychosis, experiencing significant symptoms, not to be offered antipsychotic treatment, evidence for this versus placebo dating back to the initial NIMH trial⁹. Reducing duration of untreated psychosis was one of the drivers behind FEP services, early antipsychotic treatment the cornerstone of early intervention, before formalised psychosocial interventions¹¹. Therefore, any alternatives need solid evidence before a larger trial is considered.

If symptomatic response for those assigned antipsychotics was comparable to most FEP studies, if we knew people were actually taking antipsychotics, and no worse an outcome was seen for CBT monotherapy, a larger, similar study in FEP would have been the logical next step.

Given the above, a more cautious approach should be considered- it would make sense for a larger, multi-centre trial along similar lines to the 2014 trial to take place, with addition of a psychological placebo, suggested in a commentary on that trial¹⁰. We would then be in a position to evaluate the highly relevant question of effectiveness of CBT in people not taking antipsychotic medication, laying a foundation for further study, along the lines proposed by Morrison et al.

References

- 1 Barnes TR. Evidence-based guidelines for the pharmacological treatment of schizophrenia: recommendations from the British Association for Psychopharmacology. *Journal of Psychopharmacology* 2011; **25**: 567.
- 2 Jauhar S, McKenna PJ, Radua J, Fung E, Salvador R, Laws KR. Cognitive-behavioural therapy for the symptoms of schizophrenia: systematic review and meta-analysis with examination of potential bias. *The British Journal of Psychiatry* 2014; **204**: 20–9.
- 3 Kuipers E, Yesufu-Udechuku A, Taylor C, Kendall T. Management of psychosis and schizophrenia in adults: summary of updated NICE guidance. *BMJ* 2014; **348**: g1173.
- 4 Morrison AP, Turkington D, Pyle M, *et al*. Cognitive therapy for people with schizophrenia spectrum disorders not taking antipsychotic drugs: a single-blind randomised controlled trial. *The Lancet* 2014; **383**: 1395–403.
- 5 Morrison AP, Dunn G, Turkington D, Pyle M, Hutton P. Cognitive therapy for patients with schizophrenia – Authors’ reply. *The Lancet* 2014; **384**: 401–2.
- 6 Lally J, Ajnakina O, Stubbs B, *et al*. Remission and recovery from first-episode

psychosis in adults: systematic review and meta-analysis of long-term outcome studies. *The British Journal of Psychiatry* 2017; : bjp.bp.117.201475.

7 Leucht S, Davis JM, Engel RR, Kissling W, Kane JM. Definitions of response and remission in schizophrenia: recommendations for their use and their presentation. *Acta Psychiatrica Scandinavica* 2009; **119**: 7–14.

8 Psychosis and schizophrenia in adults: treatment and management | Guidance and guidelines | NICE. <https://www.nice.org.uk/guidance/cg178> (accessed Aug 11, 2015).

9 GUTTMACHER MS. PHENOTHIAZINE TREATMENT IN ACUTE SCHIZOPHRENIA; EFFECTIVENESS: THE NATIONAL INSTITUTE OF MENTAL HEALTH PSYCHOPHARMACOLOGY SERVICE CENTER COLLABORATIVE STUDY GROUP. *Arch Gen Psychiatry* 1964; **10**: 246–61.

10 Howes O. Cognitive therapy: at last an alternative to antipsychotics? *The Lancet* 2014; **383**: 1364–6.

Dr Jauhar declares no conflict of interest

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